Câncer de próstata e Resveratrol. O resveratrol possui efeito epigenético: aumenta a acetilação do gene p53 e promove apoptose no câncer de próstata

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Possivelmente a combinação do resveratrol com inibidores da desacetilação (ácido valpróico?) possua efeitos sinérgicos, porque o resveratrol funciona de modo indireto inibindo o MTA1 (metastasis-associated protein 1). JFJ

**Resveratrol enhances p53 acetylation and apoptosis in prostate cancer by inhibiting MTA1/NuRD complex.**


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**Abstract**

Dietary compounds and epigenetic influences are well recognized factors in cancer progression. Resveratrol (Res), a dietary compound from grapes, has anticancer properties; however, its epigenetic effects are understudied. Metastasis-associated protein 1 (MTA1) is a part of the nucleosome remodeling deacetylation (NuRD) corepressor complex that mediates posttranslational modifications of histones and nonhistone proteins resulting in transcriptional repression. MTA1 overexpression in prostate cancer (PCa) correlates with tumor aggressiveness and metastasis. In this study, we have identified a novel MTA1-mediated mechanism, by which Resveratrol restores p53-signaling pathways in PCa cells. We show, for the first time, that Res causes down-regulation of MTA1 protein, leading to destabilization of MTA1/NuRD thus allowing acetylation/activation of p53. We demonstrated that MTA1 decrease by Res was concomitant with accumulation of Ac-p53. MTA1 knockdown further sensitized PCa cells to Res-dependent p53 acetylation and recruitment to the p21 and Bax promoters. Furthermore, MTA1 silencing maximized the levels of Res-induced apoptosis and pro-apoptotic Bax accumulation. HDAC inhibitor SAHA, like MTA1 silencing, increased Res-dependent p53 acetylation and showed cooperative effect on apoptosis. Our results indicate a novel epigenetic mechanism that contributes to Resveratrol anticancer activities: the inhibition of MTA1/NuRD complexes due to MTA1 decrease, which suppresses its deacetylation function and allows p53 acetylation and subsequent activation of pro-apoptotic genes. Our study identifies MTA1 as a new molecular target of Res that may have important clinical applications for PCa chemoprevention and therapy, and points to the combination of Res with HDAC inhibitors as an innovative therapeutic strategy for the treatment of PCa.

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